

Preliminary Communication

CUMULATIVE EFFECTS OF LIFETIME PASSIVE SMOKING ON CANCER RISK*

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Summary Cancer risk from cumulative household exposure to cigarette smoke was evaluated in a case-control study. Overall cancer risk rose steadily and significantly with each additional household member who smoked over an individual's lifetime. Cancer risk was also greater for individuals with exposures during both childhood and adulthood than for individuals with exposures during only one period. These trends were observed for both smoking-related and other sites. These findings are preliminary and must be confirmed with other studies. Nonetheless, they suggest that effects of exposure to the cigarette smoking of others may be greater than has been previously suspected.

INTRODUCTION

INCREASED risk of respiratory illness in children,^{1,3} changes in respiratory function in children and adults,^{4,5} risk of childhood tumours,^{6,7} and risk of lung cancer and possibly other adult cancers⁸⁻¹⁴ have all been reported as possible effects of exposure to other people's cigarette smoke (passive smoking). Adult cancer risk from childhood exposure to parents' smoking has also been discussed.^{14,15} These studies considered the independent effects of exposure in one period to cigarette smoke from only one source, even though individuals may be exposed to a number of sources over their lifetime.

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In a study of adult cancer risk related to parents' smoking¹⁵ we collected data on exposure to cigarette smoke of not only parents, but also spouses and other household members. In the present study cancer risk in relation to cumulative passive exposure to cigarette smoke was examined. We did not collect data on exposures outside the home, but were able to consider whether cancer risk increases with the number of household members who smoke.

METHODS

Study methods have been reported elsewhere.^{13,15} Cancer patients were selected from a hospital-based tumour registry. They included all those with cancer diagnosed between July 1, 1979, and March 31, 1981, and assumed to be alive on March 31, 1981. Patients ranged from 15 to 59 years of age at the time of diagnosis, and all cancer sites except basal-cell cancer of the skin were included. Patients were restricted to age 59 and younger to maximise the likelihood of maternal smoking, since few women were smokers before 1920.

Of 740 eligible cancer patients identified from the tumour registry, 107 (14%) died before we could contact them. An additional 115 (16%) either refused to participate or could not be contacted. 518 (70%) patients completed questionnaires. Control subjects were cancer-free and of the same race, sex, and age (± 5 years) as patients. They were friends or acquaintances of patients ($n=309$) or were randomly selected by systematic telephone sampling ($n=209$). Patients and control subjects were also similar in occupational category and smoking habits. Analysis was restricted to individuals who lived with both natural parents for most of the first 10 years of life. Results are reported for 369 patients and 409 control subjects who supplied information about the smoking habits of their spouse and parents.

Information on exposure to cigarette smoke was obtained by means of a structured questionnaire that was sent to all subjects. Another questionnaire was sent and follow-up telephone calls were made when a response to the first questionnaire was not obtained. Childhood exposure to cigarette smoke was assessed from questionnaire reports of smoking histories of parents and information on other household members who smoked. Subjects were considered to be exposed during childhood if one or both parents smoked cigarettes in the house before the subject was 10 years old or if one or more other household members smoked during that period. Passive exposure to cigarette smoke during adulthood was estimated from the number of years of marriage during which a spouse smoked. Subjects were considered to be exposed if they had a spouse who smoked regularly at any time during their marriage. Active smokers were defined as those who ever smoked as many as 1 cigarette a day for as long as 6 months.

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TABLE I—OVERALL CANCER RISK FROM HOUSEHOLD EXPOSURE TO CIGARETTE SMOKE

	Number of household members who smoke			
	0	1	2	3 or more
Combined group				
Patients	54	127	123	48
Control subjects	99	161	97	34
Odds ratio	1.0	1.4	2.3*	2.6*†
Active smokers‡				
Patients	22	60	78	35
Control subjects	38	73	60	25
Odds ratio	1.0	1.4	2.2*	2.4*†
Non-smokers				
Patients	32	67	45	13
Control subjects	61	88	37	9
Odds ratio	1.0	1.5	2.3*	2.8*†

*Statistically significant differences between risk with specified number of exposures and with no exposure, $p < 0.05$.

†Statistically significant χ^2 for trend, $p < 0.01$.

‡Current smokers and ex-smokers.

We have found^{13,15} that exposure to parents' or spouse's smoking contributed independently to cancer risk—ie, adjusting for one exposure did not alter the risk associated with the other. Thus we used two approaches to measure the effects of multiple exposures: cancer risk was examined in relation to the total number of household members who smoked, irrespective of when the exposures occurred, and in relation to the period during which the exposures occurred (childhood or adulthood only, or both periods). Odds ratios were calculated and a chi-square test was used to assess statistical significance. A chi-square test for linear trend was used to evaluate the risk with increasing numbers of exposures in unadjusted¹⁶ and adjusted¹⁷ analyses.

RESULTS

Cancer risk associated with exposure to increasing numbers of household members who smoke is shown in table I. A smoking mother, father, spouse, or 1 or more additional household members who smoked during the patient's childhood or a spouse who smoked while married to a patient each counted as one exposure. The total number of exposures is the sum of the individual exposures. Overall cancer risk increased significantly with increasing numbers of exposures, with odds ratios rising from 1.4 for 1 exposure to 2.3 for 2 exposures and 2.6 for 3 or more exposures. Statistically significant linear trends were also seen when smokers and non-smokers were considered separately. Adjustment for potential differences in age, race, sex, and educational level did not alter these trends.

TABLE II—OVERALL CANCER RISK FROM HOUSEHOLD EXPOSURE TO CIGARETTE SMOKE IN CHILDHOOD AND ADULTHOOD

	Age period of exposure			
	No exposure	Childhood only*	Adulthood only†	Both
Patients	54	107	58	145
Control subjects	99	124	72	98
Odds ratio	1.0	1.6‡	1.5	2.7‡§
		1.5‡		

*Exposure to smoking mother, father, or other household member during childhood.

†Exposure to smoking spouse.

‡Statistically significant differences between risk with specified exposure and no exposure, $p < 0.05$.

§Statistically significant linear trend: no exposure, exposure in only one time period, exposure in both time periods, χ^2 for trend = 23.7, $p < 0.01$.

We also measured cancer risk in relation to the period when exposures occurred (table II). Risk rose by 60% for individuals exposed during childhood only and by 50% for individuals exposed during adulthood only but was more than doubled for those exposed during childhood and adulthood (odds ratio = 2.7). There was a significant linear trend in risk for individuals exposed in no, 1, or 2 periods. Again trends were similar for smokers and non-smokers and were not affected by adjustment for potential confounding factors.

TABLE III—CANCER RISK FROM MULTIPLE HOUSEHOLD EXPOSURES TO CIGARETTE SMOKE: SITES WITH 15 OR MORE CASES*

Site	Number of cases	Number of exposures			
		0	1	2	3 or more
All sites	369	1.0	1.4	2.3	2.6‡
Smoking related†	115	1.0	1.8	3.0	3.8‡
Other	254	1.0	1.5	2.4	2.6‡
Buccal cavity and pharynx	15	1.0	4.9	5.1	2.9
Digestive tract	30	1.0	0.7	1.8	1.3
Respiratory tract	19	1.0	0.7	0.6	2.9
Breast	48	1.0	2.0	2.4	3.3‡
Cervix	62	1.0	1.6	3.6	3.4‡
Eye, brain, and other nervous system	29	1.0	2.3	2.3	0.7
Thyroid	19	1.0	1.0	3.1	8.7
Leukemia and lymphoma	37	1.0	2.5	5.1	6.8‡

*Odds ratios are given.

†Includes oral cavity and pharynx, oesophagus, pancreas, respiratory tract, urinary tract, and cervix.

‡Statistically significant linear trend.

Cancer risk increased with increasing numbers of household exposures to cigarette smoke for smoking-related sites and for other sites that are not thought to be smoking related (table III). Smoking-related sites included cancers of the oral cavity and pharynx, oesophagus, pancreas, respiratory tract, urinary tract, and cervix.^{13,18} For smoking-related sites odds ratios for 1, 2, and 3 or more exposures were 1.8, 3.0, and 3.8, respectively. The trend for the other sites combined was also statistically significant but the risk was less than that for smoking-related sites. The trends for cancers of the breast and cervix and for leukaemia and lymphoma combined were significant, but the trend for cancer of the respiratory tract was not.

DISCUSSION

If passive smoking has an effect on cancer risk the nature and extent of that risk are likely to differ for childhood and adult exposures. The clear overall trends found in this study might be associated with carcinogens present in tobacco smoke acting through multiple mechanisms at different periods of life. We found the risk of all cancers increased steadily and significantly with cumulative lifetime exposure to household members who smoke. This trend was not altered when adjustment was made for confounding variables.

Our findings must be regarded as preliminary. Prompted in part by experimental evidence¹⁹ we initially intended to measure the effect of transplacental or early childhood exposure to carcinogens on cancer risk in adulthood. We chose to investigate cigarette smoke because exposure to this carcinogen is both common and measurable. The finding of a cumulative lifetime risk from passive smoking was unexpected.

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We collected information on most possible sources of cigarette-smoke exposure that would be encountered during childhood but the only adult exposure we considered was that resulting from the smoking of a spouse. We did not validate information on smoking habits of spouses but interviewed more than 700 relatives of patients and control subjects to validate the quality of parental smoking histories provided by adult offspring. Study subjects provided adequate information on parents' smoking, and the quality of these data did not differ between patients and control subjects.

For adults in the United States exposures to cigarette smoke outside the home may be important.²⁰ Also the frequency of exposure to other people's cigarette smoke may change with age, with the peak exposure possibly occurring during a person's 20s.²⁰ We did not take exposures outside the home or age-related changes in exposure frequency into account.

Our data are limited by small numbers of any specific cancer site, by certain characteristics of our study sample, and by other features of our method.^{13,15} No conclusions about the impact of passive smoking relative to the effects of direct smoking can be made, since the selection of friends as control subjects meant they were usually matched with patients on smoking status. We confirmed the quality of our data and ruled out many, but not all, potential confounding factors.

Although the passive smoker receives a quantitatively lower exposure than the active smoker, that exposure is qualitatively richer in many smoke constituents: there is 3 times as much benzo(a)pyrene, 6 times as much toluene, and more than 50 times as much dimethylnitrosamine in a fixed volume of sidestream smoke in the gas phase as there is in cigarette smoke inhaled by the active smoker.¹⁸ The potential for damage from passive exposure may be greater than has been previously recognised.

Our finding of dose-dependent cancer risks for sites not considered to be related to active smoking might be questioned because active smokers are also passively exposed. For some sites it is not clear in the literature if no risk from direct smoking exists or if a possible link has not yet been investigated. For other sites, such as the breast, some studies have found no cancer risk associated with smoking.²¹ One possible explanation for this discrepancy is that in studies comparing smokers with non-smokers, passive smokers are included in the non-smoking group. This would make it difficult to detect a small difference in risk due to smoking. Few studies have evaluated the effects of passive smoking on risk of cancer at sites other than the lung. Furthermore, there is little data available on the effects of transplacental or childhood exposure to cigarette smoke on cancer risk in adulthood.

Data from biochemical and experimental studies support our findings though many of these reports must be regarded with caution. There is evidence that non-smokers are exposed to potential carcinogens through the cigarette smoking of others. Cigarette-smoke by-products such as cotinine and thiocyanate have been measured in the blood, urine, and saliva of non-smoking adults, children, and fetuses exposed to smokers,²²⁻²⁶ and there has been at least one report of raised levels of mutagens in urine of passive smokers.²⁷ Greater activity of enzymes that metabolise benzo(a)pyrene has been noted in placentas of smokers²⁸⁻³⁰ and even passive smokers.³¹ Similar increases may occur in tissues of fetuses, children, or adults exposed to smokers.

Studies in laboratory animals provide evidence in support of an adult cancer risk from transplacental or childhood exposure to cigarette smoke, but this hypothesis has not been

tested directly.¹⁹ Data from these studies show that many carcinogens, including those in cigarette smoke, are active when administered transplacentally or during early life and may produce effects at lower doses than those required for adults.³²⁻³⁶ Some low-dose exposures which are not in themselves carcinogenic increase the sensitivity of exposed animals to later carcinogenic exposures.^{37,38} In other experiments tumours resulting from transplacental and early postnatal exposures were not apparent until the animals were fully developed and did not necessarily differ in site or morphology from spontaneously occurring tumours.^{32,39} This is consistent with our finding of raised risk for adult tumours at many sites.

Future studies should include cancer sites not necessarily associated with active smoking and should take into account childhood sources of passive smoke exposure.

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